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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,048	01/26/2006	Philipp Hadwiger	26421-15811 US	3878
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Nixon Peabody LLP 401 9th Street N.W. Suite 900 Washington, DC 20004			EXAMINER CHONG, KIMBERLY	
			ART UNIT 1635	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/543,048	Applicant(s) HADWIGER ET AL.	
	Examiner KIMBERLY CHONG	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 21 May 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 86,94-98,100-102,110,111 and 114-119 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 86,94-98,100-102,110,111 and 114-119 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

In view of the Appeal Brief filed on 05/21/2010, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved reopening prosecution by signing below (see last page of this communication).

Status of the Application

Claims 86, 94-98, 100-102, 110, 111 and 114-119 are pending and are currently under examination. Rejections and/or objections not reiterated from the previous office action mailed 11/12/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Priority

Applicant does not receive the benefit of the earlier foreign application Germany 10302421.2 filed 01/21/2003 because the prior applications do not provide adequate support for the claims of the instant application and thus applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120.

The instant application does not receive the benefit of the earlier filed priority document because the instantly recited limitation of the logKow exceeding 1, 1.5, 2 or 3 is not recited. If Applicant believes the prior application provides support then applicant must point, with particularity, to where such support can be found in the specification of the prior application.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 86, 94-98, 100-102, 110, 111 and 114-119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, MPEP §2163 states, in part "...a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." Moreover, the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by "...disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between functional and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus."

The claims are drawn to dsRNA comprising a complementary RNA strand and a sense strand and only one lipophilic group having a logKow exceeding 1, 1.5, 2 or 3, wherein the lipophilic group is covalently attached to the 5' end of the complementary (which would be the antisense strand) wherein the dsRNA is complementary to a (+) strand RNA virus and wherein the dsRNA has the function of increased lipophilic properties.

The instant claims recite a broad genus of lipophilic groups such as steroids, branched aliphatic hydrocarbons, aromatic groups or alicyclic moieties wherein each group has a logKow exceeding 1. The specification disclose values for two lipophilic groups which are the predicted values: 6-amino hexanol and cholesteryl N-(hexan-6-ol) carbamate on page 13. The instant claims and specification fail to provide adequate written description of the infinite number of molecules claimed that are commensurate in scope with the breadth of the instant invention: having a lipophilic group exceeding 1 wherein the group is attached to a dsRNA and binds a (+) strand RNA and has the function of increased lipophilic properties.

The specification in Example 7 describes the use of a cholesteryl N-(hexan-6-ol) carbamate that is conjugated to a strand of a dsRNA and discloses this dsRNA conjugate has superior efficacy and selectivity. Disclosure of one compound having the claimed value of a logKow exceeding 1 is not adequate description for the skilled artisan to immediately envision or recognize the vast genus of different lipophilic groups that would be capable of being conjugated to a dsRNA strand and having superior efficacy and selectivity against a target gene and which have the requisite logKow.

The specification as filed does not provide specific guidance that would lead one of skill in the art to the claimed invention and the state of the art cannot provide the specific guidance because it is silent regarding the logKow values of all known compounds claimed within the genus having the required properties. Even Applicant acknowledges the logKow values of the claimed compounds vary and states "[a]s known in the art, certain sterols, steroids, and cholesterol derivatives are lipophilic to the

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degree where they have a logKow exceeding 1, while others are not." (page 10 of Appeal Brief filed 5/21/2010). The specification does not describe any structural features that would be common to members of lipophilic groups that would have the property of a lowKow exceeding 1 to constitute a description of the entire genus claimed.

MPEP §2163 states, in part "A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process." Moreover, MPEP §2163 states, in part: "[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004).

Therefore, in the instant application, Applicants have not shown possession of the entire claimed genus of lipophilic groups having a logKow exceeding 1 wherein the group is attached to a dsRNA and binds a (+) strand RNA and has the function of increased lipophilic properties.

Applicants are reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470

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(CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir.1991).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 86, 94-98, 100-102, 110, 111 and 114-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kay et al. et al. (US 2003/0139363), Fosnaugh et al. (US 2003/0143732), Manoharan, M. (Applicant's IDS 02/13/2006), MacKellar et al. (Nucleic Acids Research 1992) and evidenced by Virta (Tetrahedron 2003).

The instant claims are drawn to a dsRNA comprising a complementary RNA strand and a sense strand and only one lipophilic group having a logKow exceeding 1, 1.5, 2 or 3, wherein the lipophilic group is covalently attached to the 5' end of the complementary (which would be the antisense strand) wherein the dsRNA is complementary to a (+) strand RNA virus, wherein the linkages between the 5' comprises a phosphodiester group, wherein the linkage does not comprise a phosphodiester group, wherein the lipophilic group is a sterol, cholesteryl or selected from the group as listed in claim 98, wherein the dsRNA has overhangs on one or both

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ends, wherein the dsRNA is between 16 to 30 nucleotides in length, wherein the target gene is expressed in cells as listed in claim 117 and wherein the dsRNA targets HCV.

Kay et al. et al. teach dsRNA that efficiently inhibit viral gene expression and targeting hepatocyte cells using a dsRNA molecule is capable of inhibiting the expression of a Hepatitis C Virus (see pages 13-15).

Kay et al. et al. do not teach dsRNA comprising conjugates at the 5' end of the antisense strand, do not teach a conjugate such as a lipophilic group which has a logKow exceeding 1 and do not specifically teach the lipophilic group is linked at the 5' end with a phosphodiester group.

Fosnaugh et al. teach double-stranded RNA molecules comprising a sense and an antisense strand wherein the antisense strand is complementary to a target gene. The dsRNA taught by Fosnaugh et al. can comprise sense and antisense strands that are from 19 to 25 nucleotides in length and can further comprise nucleotide overhang regions at the 3' or 5' end (see at least pages 3-5). Fosnaugh et al. teach the dsRNA comprises a conjugate covalently attached to the dsRNA wherein the conjugate is attached at the 5' end of either strand (see paragraph 0068) and teach the conjugate can be linked with biodegradable linkers as well as phosphodiester linkages (see paragraphs 0172-0173). Fosnaugh et al. teach the conjugate molecule can be any ligand that can mediate cellular uptake of the dsRNA wherein the modifications increase the stability of the molecule and enhance the cellular uptake of the molecule which is important for *in vivo* applications (see paragraph 0032).

Manoharan teach oligonucleotides are hydrophilic and this reduces the molecules ability to permeate cells. Manoharan teach conjugation of lipophilic molecules to the terminal ends of oligonucleotides is a way to solve the cellular permeation problems (see page 106). Manoharan teach common chemical linkages (see Figure 3) and teach the use of different lipophilic groups (see Figures 5-6 and page 110). Manoharan teach conjugation of a cholesterol moiety to the 5' or 3' end of an antisense oligonucleotide studied the effects of cellular uptake and antisense efficacy. Manoharan found that the 5' and 3' cholesterol conjugates were more lipophilic than unconjugated oligonucleotides and found the 5' cholesterol conjugated or the 5', 3' cholesterol conjugated oligonucleotides had a plasma half life nearly 7 times greater than the unconjugated oligonucleotides and greater than the 3' cholesterol conjugated oligonucleotide (see page 109, column 1). Manoharan further found that the 5' cholesterol conjugated oligonucleotide was more effective at reducing target gene expression in vivo (see page 109 last paragraph to page 110). These are reasons one of ordinary skill in the art would have used lipophilic components and to attach them at the 5' end of an oligonucleotide (see also MacKellar *et al.* below).

MacKellar et al. teach that the benefits of attaching cholesterol to the 5' end of an oligonucleotide were well known in the art and teach the attachment of a cholesterol moiety, such as a cholesterol carbamate, to the terminal ends of an oligonucleotide (see page 3412).

As evidenced by Virta et al., methods of attaching conjugates to the terminal ends of an oligonucleotide were well known and attachment of a group to the 5' end is

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very straightforward as compared to attachment of the conjugate groups to the 3' end which are more complicated (see at least pp 5138-5142).

It would have been obvious to one of skill in the art to use a known oligonucleotide conjugate, such as a cholesterol group, as taught by Manoharan and MacKellar et al. to link to a dsRNA targeted to an RNA virus as taught by Kay et al. and to attach at the 5' end as taught by Fosnaugh et al. and Virta et al.

Such oligonucleotide conjugates taught by Manoharan and MacKellar et al. were known in the art at the time of filing of the instant application to provide essential benefits to oligonucleotides for the purpose of increasing cellular permeation. Manoharan summarizes the prior art and teach that oligonucleotide conjugates have been evaluated in a wide range of cell culture and in vitro experiments and the value of conjugation chemistry has been clearly demonstrated by these studies and states further that oligonucleotide conjugates improve the pharmacokinetic properties of the oligonucleotide, such as binding affinity for the target and nuclease resistance such that one can synthesize an ideal drug with predictable results.

The skilled artisan would have had an implicit motivation to conjugate a cholesterol moiety to the end of the antisense strand of a dsRNA given it was well known in the art that this lipophilic group provides serum stability to the strand as well as aids in cellular permeation. Fosnaugh et al. teach dsRNA can comprise conjugates to either the 5' end or 3' end of an antisense strand and because Manoharan teach conjugation of cholesterol to the 5' end of an antisense molecule demonstrated better serum stability and more importantly was more efficient at reducing target gene

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expression in vivo, the skilled artisan would have wanted to conjugate this group at the 5' end of the antisense strand of a dsRNA. Moreover as evidenced Virta et al., conjugation at the 5' end is a simpler process and one of skill in the art would have clearly been motivated, given all that was taught in the art regarding cholesterol, to make the claimed dsRNA with a cholesterol group attached at the 5' end with a reasonable expectation of success.

With respect to the claimed lipophilic group having a logKow exceeding 1, 1.5, 2 or 3, the cholesterol carbamate molecule taught by MacKellar is the same as instantly claimed and described in the specification on page 13 and thus this compound has the inherent property of having a logKow as instantly claimed absent evidence to the contrary.

The MPEP states:

A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

MPEP 2112.01:

PRODUCT AND APPARATUS CLAIMS WHEN THE STRUCTURE RECITED IN THE REFERENCE IS SUBSTANTIALLY IDENTICAL TO THAT OF THE CLAIMS, CLAIMED PROPERTIES OR FUNCTIONS ARE PRESUMED TO BE INHERENT

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing

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that they are not. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Therefore, because the claimed oligonucleotide conjugates were known in the art at the time of the instantly claimed invention and because such lipophilic conjugates were known to efficiently improve the cellular delivery of oligonucleotides and increase their affinity for the target gene as well as increase their resistance to nucleases, it would have been obvious to one skilled in the art to use the conjugates taught by Manoharan and MacKellar to achieve the predictable result of improvement in cellular delivery of nucleic acid molecules.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

The arguments submitted by Applicant in the Appeal Brief will be addressed with respect to the references used in the new grounds of rejection above.

Applicant argues that Fosnaugh et al. provides boilerplate language listing a large number of alternatives with respect to the conjugates and the Examiner has not presented any rationale for showing how one of ordinary skill in the art would navigate through each of the possibilities to arrive at the claimed dsRNA. In response, Fosnaugh et al. teach that it would have been obvious to attach a conjugate group via linkers to the terminal end of a dsRNA and given there are a finite number of identified predictable solutions for attaching a lipophilic group to either of 4 positions of a dsRNA, a skilled artisan would have a good reason to modified said dsRNA with a reasonable expectation of success. Moreover the above cited references provide motivation to specifically attach at the 5' end of an antisense strand. Manoharan et al. teach attachment at the 5' end provides benefits such as increased half-life in serum and better in vivo efficacy. MacKeller et al. teach it was also well known to attach at the 5' end and Virta et al. teach attachment of a conjugate to the 5' end is a simpler process than attaching at the 3' end. Thus, the skilled artisan would have implicit motivation to make the claimed dsRNA with a conjugate at the 5' end of the antisense strand.

Applicant argues the claimed invention has unexpected results such as improved activity regardless of the mechanism of entry into the cells and this improved activity is not a consequence of enhanced transport across cell membranes. In response, there is no evidence provided in the specification or by Applicant to support this assertion.

Applicant argues that Figure 3 demonstrates that the dsRNA of the claimed invention, having a lipophilic group with a logKow exceeding 1, attached at the 5' end

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achieve a 10-20% reduction in gene expression and this lipophilic group has increased lipophilic properties which is an unexpected result.

This argument is not convincing. First, while Figure 3 does in fact show a dsRNA of the claimed invention having a cholesterol attached at the 5' end and shows what appears to be a reduction of expression of a B-gal gene up to 20% as compared to the control, the data also show that the same dsRNA with a cholesterol attached at the 3' end showed an even greater reduction in gene expression as compared to the control. Thus, from the data, there does not appear to be an advantage or unexpected superior results as submitted by Applicant as the evidence does not support the arguments that conjugation of cholesterol at the 5' end allows the dsRNA to have increased uptake and unexpected results as compared to a dsRNA molecule with a conjugate at the 3' end. This discrepancy is also shown in Example 7 wherein the specifications discloses a dsRNA with a lipophilic group attached at the 5' end of the sense strand, which is not the complementary strand as claimed, had "superior efficacy and selectivity".

Thus, the results are what have been shown in the prior art and what is expected when conjugating a cholesterol group to the 5' end of an oligonucleotide: a more effective inhibitory nucleic acid molecule as compared to an unconjugated molecule. Therefore Applicant's arguments of unexpected results are not supported by the claims and instant specification.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Christopher Low at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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